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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,451	07/30/2003	Katia Vancompernolle	2676-6045US	5403

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 08/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/630,451	VANCOMPERNOLLE, KATIA	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *3-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/30/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, and 18, drawn to a phosphorylated mammalian glyoxalase I , classified in class 435, subclass 232.

II. Claims 3 and 10, drawn to a process for modulating methylglyoxal-modification of proteins, classified in class 435, subclass 4.

III. Claim 4, drawn to an a process for modulating TNF induced cell death, classified in class 435, subclass 7.71.

IV. Claims 5-9, drawn to a process for modulating stress induced cell death, classified in class 435, subclass 7.6.

V. Claim 11, drawn to a process for modifying glyoxalase I comprising phosphorylating with PKA, classified in class 435, subclass 194.

VI. Claims 12-17, drawn to a process for modulating methylglyoxal-modification of proteins in a cell, classified in class 435, subclass 7.91.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions II-VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The processes of Inventions II-VI are distinct and unrelated because they require different process steps, reagents, and parameters; have different purposes; and produce different products and/or effects.

Inventions I and (II-IV and VI) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product such as using the mammalian phosphorylated glyoxalase I in a process to make antibodies to said mammalian phosphorylated glyoxalase I.

Inventions I and V are related as process of making and product made. The inventions

are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the phosphorylated glyoxalase I can be made by another and materially different process such as using a process that uses protein kinases that are different from the recited protein kinase A (PKA), such as protein kinase C or protein kinase B, to phosphorylate the glyoxalase I.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. During a telephone conversation with Bretton L. Crockett on 8/4/2004, a provisional election was made without traverse to prosecute the invention of Group I, claims 1, 2, and 18,

drawn to a phosphorylated mammalian glyoxalase I.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Claims 1, 2, and 18, drawn to a phosphorylated mammalian glyoxalase I, are under consideration in this Office Action.

Drawings

6. Drawings submitted on 7/30/2003 are accepted by the Examiner.

Priority

7. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office (EPO) on 1/31/2001. It is noted, however, that applicant has not filed a certified copy of the EP 01200353.9 application as required by 35 U.S.C. 119(b).

Sequence Listing

8. The paper copy and computer readable form (CRF) of the Sequence Listing dated 7/30/2003 have been received and have been processed by the Scientific and Technical Information Center (STIC).

Information Disclosure Statement

9. The document, "PCT International Search Report, PCT/EP02/01118", cited in the IDS filed 7/30/2003 has been considered but has been crossed out because it is not appropriate to be printed on any patent resulting from this application.

Claim Rejections - 35 U.S.C. § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 1, 2, and 18 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 2, and 18, as written, do not sufficiently distinguish over mammalian glyoxalase I enzymes as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page 9, paragraph [0031], of the specification. See MPEP 2105.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are genus claims that are directed toward any mammalian phosphorylated glyoxalase I of any amino acid sequence and structure. The scope of the claims includes many mammalian phosphorylated glyoxalase I enzymes with widely differing structural, chemical, and physical characteristics. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted.

The specification discloses a human glyoxalase I consisting of the amino acid sequence of SEQ ID NO: 1. However, the specification fails to provide a written description of additional mammalian glyoxalase I enzymes as encompassed by the claimed genus. Neither the specification nor the general knowledge of those skilled in the art provide evidence of any partial structure which would be expected to be common to the members of the genus. Thus, the disclosed human glyoxalase I consisting of the amino acid sequence of SEQ ID NO: 1 is not representative of the claimed genus since other members of the genus have amino acid sequences and structures that are different from the said human glyoxalase I consisting of the amino acid sequence of SEQ ID NO: 1.

In view of the above considerations, one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by members of the genus since the disclosed human glyoxalase I consisting of the amino acid sequence of SEQ ID NO: 1 is not representative of the claimed genus. Accordingly, Applicant has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention.

Claim Rejections - 35 U.S.C. § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1, 2, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ranganathan et al. (J Biol Chem. 1993 Mar 15;268(8):5661-7; PTO 1449) in view of Pestka et al. (Protein Expr Purif. 1999 Nov;17(2):203-14; PTO 892).

Ranganathan et al. teach the human colon glyoxalase I which is a mammalian glyoxalase I enzyme that has an amino acid sequence that is 100 % identical to SEQ ID NO: 1 (see enclosed alignment Accession A46714) and has four possible phosphorylation sites (2 serine and 2 threonine) (see entire publication, especially p. 5663, left column, 2nd full paragraph).

The invention of claims 1, 2, and 18 differs from the teachings of the reference only in

that the human glyoxalase I taught by Ranganathan et al. is not phosphorylated.

Pestka et al. teach (1) various methods for phosphorylating proteins by introducing protein kinase recognition sites into any protein and subsequent phosphorylation of the protein with radioisotopes ^{32}P or ^{33}P through the action of protein kinases or by directly phosphorylating proteins that already contain protein kinase recognition sites with radioisotopes ^{32}P or ^{33}P through the action of protein kinases, (2) the methods can be applied to virtually all proteins, (3) introduction of a kinase recognition site allows proteins to keep their essential structure intact, and (4) the advantage that these phosphorylated proteins are useful in a wide variety of applications, such as pharmocokinetics, localization, and diagnostic imaging (see entire publication, especially pp.203-206, and p.211 **Concluding Remarks**).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to phosphorylate the human glyoxalase I as taught by Ranganathan et al. using the methods for phosphorylating proteins taught by Pestka et al. to create a phosphorylated human glyoxalase I having an amino acid sequence that is 100% identical to SEQ ID NO: 1, wherein its four possible phosphorylation sites (2 serine and 2 threonine) are phosphorylated with radioisotopes ^{32}P or ^{33}P through the action of protein kinases; or a protein kinase recognition site is introduced into the said human glyoxalase I and then the said human glyoxalase I is phosphorylated with radioisotopes ^{32}P or ^{33}P through the action of protein kinases.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this so that the phosphorylated human glyoxalase I can then be used in a wide variety of applications as taught by Pestka et al. including pharmocokinetics, localization, and diagnostic imaging of the phosphorylated human glyoxalase I, and that introduction of a kinase recognition site allows proteins to keep their essential structure intact.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for success for making a phosphorylated human glyoxalase I because Pestka et al. teach that the stated methods for phosphorylating proteins with protein kinase recognition sites can be applied to virtually all proteins.

Claim 18 is included in this rejection because claim 18 is a product by process claim. MPEP §2113 states:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966

(Fed. Cir. 1985).

In view of MPEP §2113, claim 18 is deemed to only encompass any phosphorylated mammalian glyoxalase I, and is not limited by the process steps of making the phosphorylated mammalian glyoxalase I. The process steps do not impart any unique structural or chemical properties and limitations to the recited phosphorylated mammalian glyoxalase I.

Thus, the phosphorylated mammalian glyoxalase I of claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ranganathan et al. in view of Pestka et al. for the reasons stated above.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christian L. Fronda
Art Unit 1652
August 9, 2004